Scientific Abstract

This is a Phase Ib, open-label, single arm gene transfer clinical trial of AdV-tk + valacyclovir in combination with standard-of-care surgery and/or radiation therapy for newly diagnosed patients with malignant gliomas. The rationale for this research is based on preclinical studies demonstrating improved efficacy without added toxicity when the AdV-tk gene transfer approach is combined with surgery or radiation therapy. The approach is further justified by the poor prognosis from current therapeutic approaches for malignant gliomas. A completed phase I study of AdV-tk + prodrug as a mono-therapy approach in recurrent malignant gliomas demonstrated a safe dose range for AdV-tk in brain tumors and some encouraging results. AdV-tk has been well tolerated in combination with radiation therapy in over 70 patients in an ongoing Phase II study for prostate cancer. Since AdV-tk combined with radiotherapy has not been evaluated in the brain, this dose escalation study will be performed to determine the safe dose of AdV-tk when used in combination with radiation therapy in brain tumors. The primary objective for this Phase Ib study is to evaluate the safety of escalating doses of AdV-tk with a fixed dose of the oral prodrug valacyclovir and standard of care for malignant gliomas. Information gained from this trial will be used to determine the appropriate AdV-tk dose for a subsequent Phase II study to evaluate potential efficacy of this approach in malignant brain tumors.